Attorney Docket No.: DEX-0241
Inventors: Recipon et al.
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Amendments to the specification:

Please replace the paragraph at page 48, lines 25-29 with the following:

Expression control sequences for yeast cells, typically *S. cerevisiae*, will include a yeast promoter, such as the CYC1 promoter, the GAL1 promoter, the GAL10 promoter, ADH1 promoter, the promoters of the yeast $\underline{\alpha}$-mating system, or the GPD promoter, and will typically have elements that facilitate transcription termination, such as the transcription termination signals from the CYC1 or ADH1 gene.

Please replace the paragraph at page 54, lines 2-19 with the following:

Polypeptides of the invention may be post-translationally modified. Post-translational modifications include phosphorylation of amino acid residues serine, threonine and/or tyrosine, N-linked and/or O-linked glycosylation, methylation, acetylation, prenylation, methylation, acetylation, arginylation, ubiquination and racemization. One may determine whether a polypeptide of the invention is likely to be post-translationally modified by analyzing the sequence of the polypeptide to determine if there are peptide motifs indicative of sites for post-translational modification. There are a number of computer programs that permit prediction of post-translational modifications. See, e.g., ~~www.expasy.org~~ expasy.org of the world wide web (accessed August 31, 2001), which includes PSORT, for prediction of protein sorting signals and localization sites,

SignalP, for prediction of signal peptide cleavage sites, MITOPROT and Predotar, for prediction of mitochondrial targeting sequences, NetOGlyc, for prediction of type O-glycosylation sites in mammalian proteins, big-PI Predictor and DGPI, for prediction of prenylation-anchor and cleavage sites, and NetPhos, for prediction of Ser, Thr and Tyr phosphorylation sites in eukaryotic proteins. Other computer programs, such as those included in GCG, also may be used to determine post-translational modification peptide motifs.

Please replace the paragraph at page 54, lines 20-31 with the following:

General examples of types of post-translational modifications may be found in web sites such as the Delta Mass database ~~http://www.abrf.org/ABRF/Research Committees/deltamass/deltamass.html~~ abrf.org/ABRF/Research Committees/ deltamass/deltamass.html of the world wide web (accessed October 19, 2001); "GlycoSuiteDB: a new curated relational database of glycoprotein glycan structures and their biological sources" Cooper et al. Nucleic Acids Res. 29; 332-335 (2001) and ~~http://www.glycosuite.com/~~ glycosuite.com/ of the world wide web (accessed October 19, 2001); "O-GLYCBASE version 4.0: a revised database of O-glycosylated proteins" Gupta et al. Nucleic Acids Research, 27: 370-372 (1999) and ~~http://www.cbs.dtu.dk/databases/OGLYCBASE/~~ cbs.dtu.dk/databases/OGLYCBASE/ of the world wide web(accessed October 19, 2001); "PhosphoBase, a database of phosphorylation sites: release 2.0.", Kreegipuu et al. Nucleic Acids Res

27(1):237-239 (1999) and ~~http://www.cbs.dtu.dk/databases/PhosphoBase/~~ cbs.dtu.dk/ databases/PhosphoBase/ of the world wide web (accessed October 19, 2001); or ~~http://pir.georgetown.edu/ pirwww/search/textresid.html~~ pir.georgetown.edu/pirwww/search/textresid.html of the world wide web (accessed October 19, 2001).

Please replace the paragraph at page 56, line 25 through page 57, line 14 with the following:

In another embodiment, the invention provides polypeptides that have been post-translationally modified. In one embodiment, polypeptides may be modified enzymatically or chemically, by addition or removal of a post-translational modification. For example, a polypeptide may be glycosylated or deglycosylated enzymatically. Similarly, polypeptides may be phosphorylated using a purified kinase, such as a MAP kinase (e.g, p38, ERK, or JNK) or a tyrosine kinase (e.g., Src or erbB2). A polypeptide may also be modified through synthetic chemistry. Alternatively, one may isolate the polypeptide of interest from a cell or tissue that expresses the polypeptide with the desired post-translational modification. In another embodiment, a nucleic acid molecule encoding the polypeptide of interest is introduced into a host cell that is capable of post-translationally modifying the encoded polypeptide in the desired fashion. If the polypeptide does not contain a motif for a desired post-translational modification, one may alter the post-translational modification by mutating the nucleic acid sequence of a nucleic acid molecule encoding the polypeptide so

that it contains a site for the desired post-translational modification. Amino acid sequences that may be post-translationally modified are known in the art. See, e.g., the programs described above on the website ~~www.expasy.org~~ expasy.org of the world wide web. The nucleic acid molecule is then be introduced into a host cell that is capable of post-translationally modifying the encoded polypeptide. Similarly, one may delete sites that are post-translationally modified by either mutating the nucleic acid sequence so that the encoded polypeptide does not contain the post-translational modification motif, or by introducing the native nucleic acid molecule into a host cell that is not capable of post-translationally modifying the encoded polypeptide.

Please replace the paragraph at page 59, line 20 through page 60, line 2 with the following:

Plasmid vectors will typically be introduced into chemically competent or electrocompetent bacterial cells. *E. coli* cells can be rendered chemically competent by treatment, e.g., with $CaCl_2$, or a solution of Mg^{2+}, Mn^{2+}, Ca^{2+}, Rb^{+} or K^{+}, dimethyl sulfoxide, dithiothreitol, and hexamine cobalt (III), Hanahan, J. Mol. Biol. 166(4):557-80 (1983), and vectors introduced by heat shock. A wide variety of chemically competent strains are also available commercially (e.g., Epicurian Coli® XL10-Gold® Ultracompetent Cells (Stratagene, La Jolla, CA, USA); DH5α competent cells (Clontech Laboratories, Palo Alto, CA, USA); and TOP10 Chemically Competent E. coli Kit (Invitrogen, Carlsbad, CA, USA)). Bacterial cells can be rendered electrocompetent, that is,

competent to take up exogenous DNA by electroporation, by various pre-pulse treatments; vectors are introduced by electroporation followed by subsequent outgrowth in selected media. An extensive series of protocols is provided online in Electroprotocols (BioRad, Richmond, CA, USA) (~~http://www.biorad.com/LifeScience/pdf/ New_Gene_Pulser.pdf~~ biorad.com/LifeScience/pdf/ New_Gene_Pulser.pdf of the world wide web).

Please replace the paragraph at page 60, line 25 through page 61, line 10 with the following:

Mammalian and insect cells can be directly infected by packaged viral vectors, or transfected by chemical or electrical means. For chemical transfection, DNA can be coprecipitated with $CaPO_4$ or introduced using liposomal and nonliposomal lipid-based agents. Commercial kits are available for $CaPO_4$ transfection (CalPhos™ Mammalian Transfection Kit, Clontech Laboratories, Palo Alto, CA, USA), and lipid-mediated transfection can be practiced using commercial reagents, such as LIPOFECTAMINE™ 2000, LIPOFECTAMINE™ Reagent, CELLFECTIN® Reagent, and LIPOFECTIN® Reagent (Invitrogen, Carlsbad, CA, USA), DOTAP Liposomal Transfection Reagent, FuGENE 6, X-tremeGENE Q2, DOSPER, (Roche Molecular Biochemicals, Indianapolis, IN USA), Effectene™, PolyFect®, Superfect® (Qiagen, Inc., Valencia, CA, USA). Protocols for electroporating mammalian cells can be found online in Electroprotocols (Bio-Rad, Richmond, CA, USA) (~~http://www.bio-rad.com/LifeScience/pdf/ New_Gene_Pulser.pdf~~ bio-rad.com/LifeScience/pdf/ New_Gene_Pulser.pdf of the world

wide web); Norton et al. (eds.), Gene Transfer Methods: Introducing DNA into Living Cells and Organisms, BioTechniques Books, Eaton Publishing Co. (2000); incorporated herein by reference in its entirety. Other transfection techniques include transfection by particle bombardment and microinjection. See, e.g., Cheng et al., Proc. Natl. Acad. Sci. USA 90(10): 4455-9 (1993); Yang et al., Proc. Natl. Acad. Sci. USA 87(24): 9568-72 (1990).